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File 155:MEDLINE(R) 1966-2002/Feb W3

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S5 3 S1 AND S4
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3/7/7
DIALOG(R)File 155:MEDLINE(R)
10800731 99126539 PMID: 9925788
NMR structure of the (52-96) C-terminal domain of the HIV-1 regulatory protein Vpr: molecular insights into its biological functions.
Schuler W; Wecker K; de Rocquigny H; Baudat Y; Sire J; Roques BP
INSERM U266 - CNRS UMR 8600, UFR des Sciences Pharmaceutiques et Biologiques, 4, avenue de l'Observatoire, Paris Cedex 06, 75270, France.
Journal of molecular biology (ENGLAND) Feb 5 1999, 285 (5) p2105-17, ISSN 0022-2836 Journal Code: J6V
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
The HIV-1 regulatory protein Vpr (96 amino acid residues) is incorporated into the virus particle through a mechanism involving its interaction with the C-terminal portion of Gag. Vpr potentiates virus replication by interrupting cell division in the G2 phase and participates in the nuclear transport of proviral DNA. The domain encompassing the 40 C-terminal residues of Vpr was shown to be involved in cell cycle arrest and binding of nucleocapsid protein NCp7, and suggested to promote nuclear provirus transfer. Accordingly, we show here that the synthetic 52-96 but not 1-51 sequences of Vpr interact with HIV-1 RNA. Based on these results, the structure of (52-96)Vpr was analysed by two-dimensional 1H-NMR in aqueous TFE (30%) solution and refined by restrained molecular dynamics. The structure is characterized by a long (53-78) amphipathic alpha-helix, followed by a less defined (79-96) C-terminal domain. The Leu60 and Leu67 side-chains are located on the hydrophobic side of the helix, suggesting their involvement in Vpr dimerization through a leucine zipper-type mechanism. Accordingly, their replacement by Ala eliminates Vpr dimerization in the two hybrid systems, while mutations of Ile74 and Ile81 have no effect. This was confirmed by gel filtration measurements and circular dichroism, which also showed that the alpha-helix still exists in (52-96)Vpr and its Ala60, Ala67 mutant in the presence and absence of TFE. Based on these results, a model of the coiled-coil Vpr dimer has been described, and its biological relevance as well as that of the structural characteristics of the 52-96 domain for the different functions of Vpr, including HIV-1 RNA binding, are discussed. Copyright 1999 Academic Press.
Record Date Created: 19990325

3/7/8
DIALOG(R)File 155:MEDLINE(R)
10758555 99066695 PMID: 9851370
Solution structure of peptides from HIV-1 Vpr protein that cause membrane permeabilization and growth arrest.
Yao S; Torres AM; Azad AA; Macreadie IG; Norton RS
Biomolecular Research Institute, Parkville, Victoria, Australia.
Journal of peptide science (ENGLAND) Nov 1998, 4 (7) p426-35, ISSN 1075-2617 Journal Code: CWH
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Vpr, one of the accessory gene products encoded by HIV-1, is a 96-residue protein with a number of functions, including targeting of the viral pre-integration complex to the nucleus and inducing growth arrest of dividing cells. We have characterized by 2D NMR the solution conformations of bioactive synthetic peptide fragments of Vpr encompassing a pair of H(F/S)RIG sequence motifs (residues 71-75 and 78-82 of HIV-1 Vpr) that cause cell membrane permeabilization and death in yeast and mammalian cells. Due to limited solubility of the peptides in water, their structures were studied in aqueous trifluoroethanol. Peptide Vpr59-86 (residues 59-86 of Vpr) formed an alpha-helix encompassing residues 60-77, with a kink in the vicinity of residue 62. The first of the repeated sequence motifs (HFRIG) participated in the well-defined alpha-helical domain whereas the second (HSRIG) lay outside the helical domain and formed a reverse turn followed by a less ordered region. On the other hand, peptides Vpr71-82 and Vpr71-96, in which the sequence motifs were located at the N-terminus, were largely unstructured under similar conditions, as judged by their C(alpha)H chemical shifts. Thus, the HFRIG and HSRIG motifs adopt alpha-helical and turn structures, respectively, when preceded by a helical structure, but are largely unstructured in isolation. The implications of these findings for interpretation of the structure-function relationships of synthetic peptides containing these motifs are discussed.
Record Date Created: 19990301

3/7/17
DIALOG(R)File 155:MEDLINE(R)
09723699 98205790 PMID: 9535734
Structural studies of synthetic peptide fragments derived from the HIV-1 Vpr protein.
Luo Z; Butcher DJ; Murali R; Srinivasan A; Huang Z
Kimmel Cancer Institute, Jefferson Medical College, Thomas Jefferson University, Philadelphia, Pennsylvania 19107, USA. zhuang@nana.jci.tju.edu
Biochemical and biophysical research communications (UNITED STATES) Mar 27 1998, 244 (3) p732-6, ISSN 0006-291X Journal Code: 9Y8
Contract/Grant No.: AI29306, AI, NIAID
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Vpr, one of the accessory gene products of the human immunodeficiency virus-1 (HIV-1) genome, exhibits diverse biological characteristics. Vpr functions as a transcriptional activator of HIV and heterologous promoters. It is capable of arresting cells in cell cycle progression and plays a crucial role in the infection of macrophages. Despite the wealth of information available on the biological aspects of Vpr, the structure of Vpr remains poorly understood. To gain insight into the structure-function relationship of Vpr, peptides corresponding to putative helical regions of Vpr were synthesized and their structures determined by circular dichroism (CD) spectroscopy. The CD studies confirmed the predicted helical structures of these peptides. Based on the data, a hypothetical model for the structure of Vpr was proposed which displays an anti-parallel alpha-helix core structure reminiscent of a helix-loop-helix motif. These findings are consistent with the results from mutational studies of Vpr and provide a plausible structural basis to further investigate the multiple functions of Vpr as a viral protein.
Record Date Created: 19980504

3/7/23
DIALOG(R)File 155:MEDLINE(R)
08409672 94267704 PMID: 8207641
Induction of neutralizing antibodies against human immunodeficiency virus type 1 using synthetic peptide constructs containing an immunodominant T-helper cell determinant from vpr.
Sarobe P; Lasarte JJ; Golvano JJ; Prieto I; Gullon A; Soto MJ; Labarga P; Prieto J; Borras-Cuesta F
Departamento de Medicina Interna, Universidad de Navarra, Pamplona, Spain.
Journal of acquired immune deficiency syndromes (UNITED STATES) Jul 1994, 7 (7) p635-40, ISSN 0894-9255 Journal Code: JOF
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Identification of immunodominant T-helper-cell determinants after natural infection is an important step in the design of immunogens for potential use in vaccination. Using cells from human immunodeficiency virus type 1 (HIV-1)-infected individuals and a panel of peptides encompassing the sequence of the regulatory protein vpr from HIV-1, we identified the T-helper determinant QLLFIHFRIGCRHSR, which is active in 37.5% of these individuals. To gain insight on the efficacy of this peptide in helping induce neutralizing antibodies against a B-cell determinant (BD), we synthesized constructs containing B- and T-cell determinants and tested them in BALB/c mice, the highest responders to the T-cell determinant moiety among several strains tested. These immunogens induced antibodies against two chosen B-cell determinants from HIV-1IIIB gp160 (amino acids 310-322 from the V3 loop of gp120 and 736-751 from gp41) that were able to neutralize HIV-1 infection in vitro. The highest neutralization titer against HIV-1IIIB was obtained by immunization with the homopolymer of the construct containing the T-cell epitope from vpr and the B-cell epitope from the V3 loop. We believe that the immunodominant T-cell determinant from vpr is a promising epitope to consider in the design of future peptide vaccines.
Record Date Created: 19940712

3/7/25
DIALOG(R)File 155:MEDLINE(R)
07359236 91122920 PMID: 2149126
A synthetic protein corresponding to the entire vpr gene product from the human immunodeficiency virus HIV-1 is recognized by antibodies from HIV-infected patients.
Gras-Masse H; Ameisen JC; Boutillon C; Gesquiere JC; Vian S; Neyrinck JL; Drobecq H; Capron A; Tartar A
Biomolecular Chemistry Facility, CNRS-1309, Pasteur Institute, Lille, France.
International journal of peptide and protein research (DENMARK) Sep 1990, 36 (3) p219-26, ISSN 0367-8377 Journal Code: GSD
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
The 95 amino acid-protein encoded by the non-structural vpr gene of the human immunodeficiency virus type 1 (LAV-1BRU isolate) was chemically synthesized by solid phase methodology. The synthetic vpr protein was characterized by amino acid analysis, sequence analysis, RP-HPLC, and urea-SDS PAGE. Using a radioimmunoassay, antibodies to the synthetic protein were detected in sera of 25% of HIV 1-seropositive patients tested. Western blot analysis suggested that the antibodies preferentially recognize the dimeric form of vpr.
Record Date Created: 19910314
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1/7/1
DIALOG(R)File 155:MEDLINE(R)
12866632 21657437 PMID: 11799157
Nef-mediated resistance of human immunodeficiency virus type 1 to antiviral cytotoxic T lymphocytes.
Yang Otto O; Nguyen Phuong Thi; Kalams Spyros A; Dorfman Tanya; Gottlinger Heinrich G; Stewart Sheila; Chen Irvin S Y; Threlkeld Steven; Walker Bruce D
Division of Infectious Diseases and AIDS Institute, UCLA Medical Center, Los Angeles, California 90095, USA. oyang@mednet.ucla.edu
Journal of virology (United States) Feb 2002, 76 (4) p1626-31, ISSN 0022-538X Journal Code: 0113724
Contract/Grant No.: AI43203, AI, NIAID
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Although Nef has been proposed to effect the escape of human immunodeficiency virus type 1 (HIV-1) from cytotoxic T lymphocytes (CTL) through downmodulation of major histocompatibility complex class I molecules, little direct data have been presented previously to support this hypothesis. By comparing nef-competent and nef-deleted HIV-1 strains in an in vitro coculture system, we demonstrate that the presence of this viral accessory gene leads to impairment of the ability of HIV-1-specific CTL clones to suppress viral replication. Furthermore, inhibition by genetically modified CTL that do not require major histocompatibility complex class I-presented antigen (expressing the CD4 T-cell receptor [TCR] zeta-chain hybrid receptor) is similar for both nef-competent and -deleted strains, indicating that Nef does not impair the effector functions of CTL but acts at the level of TCR triggering. In contrast, we note that another accessory gene, vpr, does not induce resistance of HIV-1 to suppression by CTL clones. We conclude that Nef (and not Vpr) contributes to functional HIV-1 immune evasion and that this effect is mediated by diminished antigen presentation to CTL.
Record Date Created: 20020118
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5/7/1
DIALOG(R)File 155:MEDLINE(R)
10841624 20493584 PMID: 10903315
Functional and structural characterization of synthetic HIV-1 Vpr that transduces cells, localizes to the nucleus, and induces G2 cell cycle arrest.
Henklein P; Bruns K; Sherman MP; Tessmer U; Licha K; Kopp J; de Noronha CM; Greene WC; Wray V; Schubert U
Humboldt University, Institute of Biochemistry, 10115 Berlin, Germany.
Journal of biological chemistry (UNITED STATES) Oct 13 2000, 275 (41) p32016-26, ISSN 0021-9258 Journal Code: HIV
Contract/Grant No.: R01 AI45324, AI, NIAID
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Human immunodeficiency virus (HIV) Vpr contributes to nuclear import of the viral pre-integration complex and induces G(2) cell cycle arrest. We describe the production of synthetic Vpr that permitted the first studies on the structure and folding of the full-length protein. Vpr is unstructured at neutral pH, whereas under acidic conditions or upon addition of trifluorethanol it adopts alpha-helical structures. Vpr forms dimers in aqueous trifluorethanol, whereas oligomers exist in pure water. (1)H NMR spectroscopy allows the signal assignment of N- and C-terminal amino acid residues; however, the central section of the molecule is obscured by self-association. These findings suggest that the in vivo folding of Vpr may require structure-stabilizing interacting factors such as previously described interacting cellular and viral proteins or nucleic acids. In biological studies we found that Vpr is efficiently taken up from the extracellular medium by cells in a process that occurs independent of other HIV-1 proteins and appears to be independent of cellular receptors. Following cellular uptake, Vpr is efficiently imported into the nucleus of transduced cells. Extracellular addition of Vpr induces G(2) cell cycle arrest in dividing cells. Together, these findings raise the possibility that circulating forms of Vpr observed in HIV-infected patients may exert biological effects on a broad range of host target cells.
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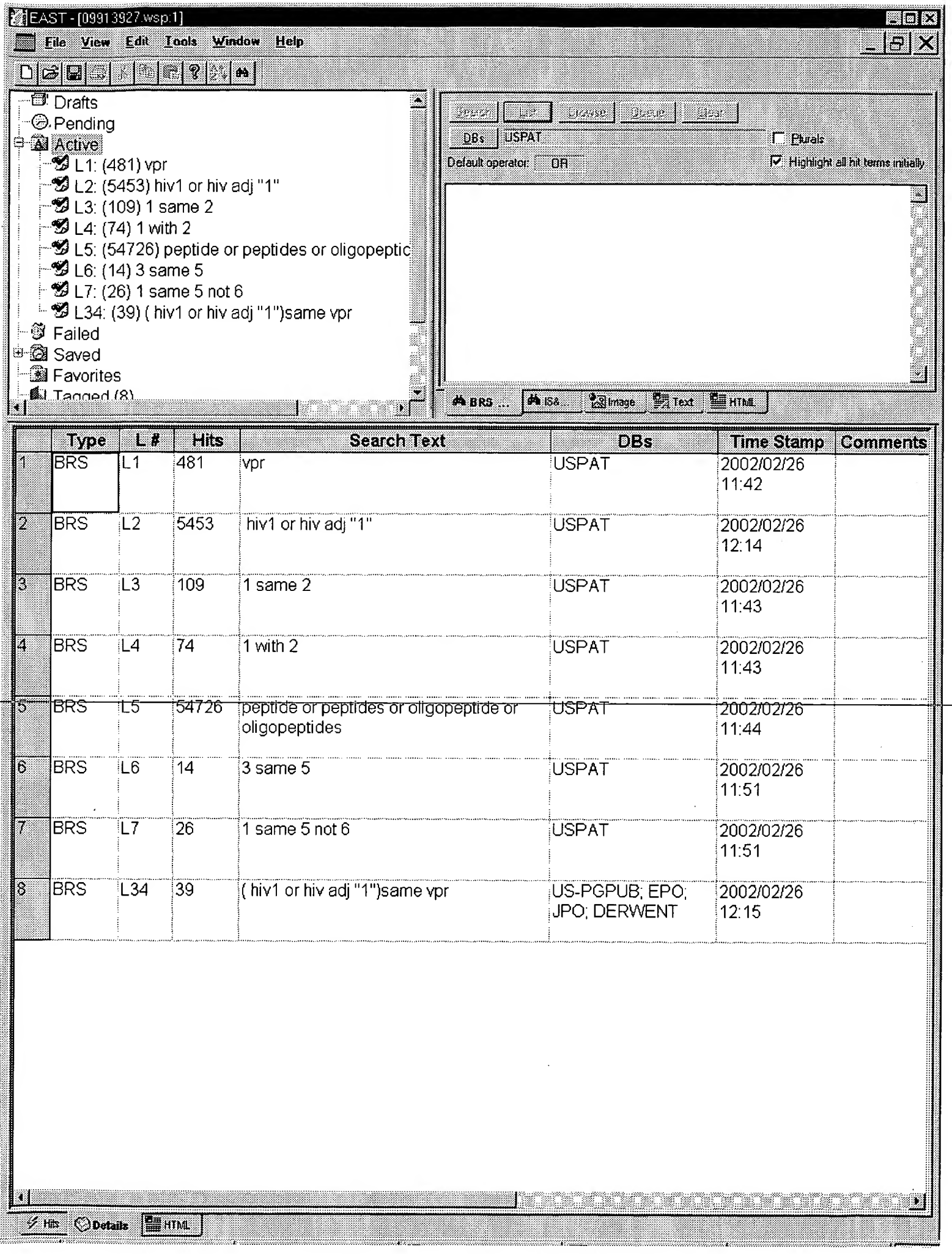

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2	BRS	L2	5453	hiv1 or hiv adj "1"	USPAT	2002/02/26 12:14	
3	BRS	L3	109	1 same 2	USPAT	2002/02/26 11:43	
4	BRS	L4	74	1 with 2	USPAT	2002/02/26 11:43	
5	BRS	L5	54726	peptide or peptides or oligopeptide or oligopeptides	USPAT	2002/02/26 11:44	
6	BRS	L6	14	3 same 5	USPAT	2002/02/26 11:51	
7	BRS	L7	26	1 same 5 not 6	USPAT	2002/02/26 11:51	
8	BRS	L34	39	(hiv1 or hiv adj "1")same vpr	US-PGPUB; EPO; JPO; DERWENT	2002/02/26 12:15	